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Retrospective study about using topotecan in second-line treatment of small-cell lung cancer. Experience of a single institution, from 2002 to 2006

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Introduction: Small-cell lung cancer (SCLC) accounts for about 20% of all lung cancers and it has poor prognosis. For extensive disease (ED), combination chemotherapy (CT) with platinum and etoposide is standard, with response rate of 60-80%, but the overall long-term survival is less than 10% (at 5 years) with a median progression-free survival of 4 months. Topotecan produces a response rate of about 24% in sensitive relapse patients (pts).

Material and Methods: The authors reviewed 146 consecutive pts with SCLC, diagnosed from January of 2002 to December of 2006, at Portuguese Institute of Oncology - Porto Center, and they evaluated those treated with topotecan as second-line CT, regarding topotecan's efficacy and toxicity.

Results: From 146 pts reviewed, 23 were treated with topotecan as second-line CT. 91% were male, the median age was 59 years (range: 23-73) and all of them were smokers or ex-smokers. At time of diagnosis, 78% had ED treated with platinum and etoposide; 22% had limited disease treated with platinum and etoposide plus thoracic radiotherapy. The median time from first line treatment to progression was 7.6 months. At beginning of second-line treatment with topotecan, 74% had a performance status (PS) less than 2 and 26% had a PS of 2. It was used the standard regimen i.v. topotecan at a dose of 1,5 mg/m^2 on days 1-5 of a 21 day cycle. The mean of number of cycles of topotecan done was 3.4 with a range of 1 to 6. Topotecan's disease control was 31.8% (partial response - 4 pts, stable disease - 3 pts) and median time to progression was 2.6 months. Topotecan grade 3 toxicities described were: anemia in 5 pts, trombocitopenia in 4 pts, neutropenia in 3 pts and vomiting in 1 pt. It was described 2 cases of febrile neutropenia. Median overall survival was 18.2 months.

Conclusion: Topotecan has clinical activity in pts with relapsed SCLC, with acceptable toxicity. In this serie of our current daily practice pts, disease control, median time to progression and median overall survival were comparable to other published results.

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Evaluation of the Recommended Dose and Efficacy of Amrubicin as 2nd and 3rd-line Chemotherapy for Small-Cell Lung Cancer

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Background: After successful induction therapy for small-cell lung cancer (SCLC), most patients relapse within 2 years as a result of emergence of drug-resistant tumor cells. This study was conducted to evaluate the recommended dose and activity of amrubicin (AMR) as 2nd-or 3rd-line chemotherapy for SCLC.

Methods: SCLC patients with measurable disease who had previously been treated with at least one platinum-based chemotherapy regimen and had an ECOG performance status of 0-2 were eligible. Two groups of patients were selected: i) a group to be treated with 2nd-line chemotherapy and ii) a group to be treated with 3rd-line chemotherapy. AMR was administered to both groups as a 5-minute daily intravenous injection of a dose of 40 mg/m^2 or 35 mg/m^2 for 3 consecutive days, every 3 weeks.

Results: Between March 2003 and June 2006, 27 patients (2nd-line, 40mg/m^2: 13; 3rd-line, 40mg/m^2: and 35 mg/m^2: 7) were enrolled. Although the 40 mg/m^2 dose of AMR was feasible (1/13 febrile neutropenia and 4/13 grade 4 neutropenia) and effecitive (6/13 PR) in the 2nd-line group, it had unacceptable toxicity in a 3rd-line setting (3/7 grade 3 non-hematologic toxicities [febrile neutorpenia:2; fatigue:1] and 4/7 grade 4 neutropenia). The 35 mg/m^2 dose of AMR had acceptable toxicity in the 3rd-line group (1/7 febrile neutropenia, 1/7 grade 4 nerutropenia) and moderate efficacy (1/7 PR, 2/7 SD).

Conclusion: AMR exhibits significant activity as 2nd-line or 3rd-line chemotherapy for SCLC. The recommended dose is 40 mg/m^2 in a 2nd-line setting and 35 mg/m^2 in a 3rd-line setting.

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A Phase II study of belotecan (CKD-602), Camtobell in patients with SCLC

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Background: Small cell lung cancer is one of cancers with high mortality rate. Etoposide/cisplatin and recently irinotecan/cisplatin have shown an excellent anti-tumor effect against SCLC. However, short response duration and rare long-term survival have been characterized although it has high response to combination chemotherapy. CKD-602 (Belotecan) is a new camptothecin derivative anti-tumor agent that belongs to the topoisomerase inhibitors developed by Chong Kun Dang pharmaceutical company in Korea. Preclinical studies suggest that it may have greater anti-tumor activity and lower toxicity than other camptothecin anticancer agents.

Methods: Patients with limited stage SCLC which progressed after it had responded to prior chemotherapy or extensive stage SCLC, were included. Patients with no measurable lesions, prior chemotherapy with topoisomerase inhibitor such as topotecan and irinotecan were excluded. The dose and schedule of CKD-602 at 1st cycle was 0.5mg/m^2/day for 30 min every 3 weeks and then the dose was modified according to the toxicity.

Results: From March 2005 to August 2006, the total numbers of registered patients were 75. Among them, 71 patients were evaluable for the toxicity, 50 for the response. Mean cycle was 3.7 (range, 1 - 9). The response rate was 69% for 1st line chemotherapy, and 33.3% for 2nd line chemotherapy. 73.2% and 25.3% of patients experienced grade 3-4 neutropenia and thrombocytopenia, respectively, without a treatment-related death.

Conclusion: CKD-602 (Belotecan), a new camptothecin analogue, showed activity and acceptable toxicities as a single agent in patients with SCLC. This study suggests that CKD-602 can be used as treatment with promising response rates in SCLC.